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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Sang Yup Lee

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INTELLECTUAL PROPERTY / TECHNOLOGY LAW

PO BOX 14329

RESEARCH TRIANGLE PARK, NC 27709

EXAMINER

JUNG, UNSU

ART UNIT

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1641

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/541,261	<b>Applicant(s)</b> LEE ET AL.	
	<b>Examiner</b> UNSU JUNG	<b>Art Unit</b> 1641	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 December 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 4-12 is/are pending in the application.
- 4a) Of the above claim(s) 8 and 10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,4-7 and 9 is/are rejected.
- 7) ☒ Claim(s) 11 and 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/17/2009</u> .  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on December 17, 2009 has been entered. The submission included new claims 11 and 12.

### ***Status of Claims***

2. Claims 1 and 4-12 are pending, claims 8 and 10 have been withdrawn from consideration, and claims 1, 4-7, 9, 11, and 12 are currently under consideration for patentability under 37 CFR 1.104.

### ***Priority***

3. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). This application is the U.S. national stage application of International PCT Application No. PCT/KR2003/002183, filed on October 18, 2003, which claims the priority of Korean Patent Application Serial No. 10/2003/0000464, filed on January 4,

2003. The certified copy of Korean Patent Application Serial No. 10/2003/0000464 has been filed in the instant application.

***Information Disclosure Statement***

4. The information disclosure statement filed on December 17, 2009 has been considered by the examiner.

***Rejections Withdrawn***

5. Upon further consideration, the following rejections have been withdrawn in favor of the new grounds of rejections set forth below:

- Rejection of claims 1 and 4-6 under 35 U.S.C. 103(a) as being unpatentable over MacBeath et al. (*Science*, Sept. 8, 2000, Vol. 289, pp1760-1763) in view of Inglese et al. (U.S. Patent No. 6,335,176 B1, Jan. 1, 2002); and
- Rejection of claims 7 and 9 under 35 U.S.C. 103(a) as being unpatentable over MacBeath et al. (*Science*, Sept. 8, 2000, Vol. 289, pp1760-1763) in view of Inglese et al. (U.S. Patent No. 6,335,176 B1, Jan. 1, 2002), and further in view of Duffy (U.S. PG Pub. No. US 2002/0028463 A1, Mar. 7, 2002).

***New Grounds of Rejections***

***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacBeath et al. (*Science*, Sept. 8, 2000, Vol. 289, pp1760-1763) (hereinafter "MacBeath") in view of Inglese et al. (U.S. Patent No. 6,335,176 B1, Jan. 1, 2002) (hereinafter "Inglese"), Shipwash (U.S. PG Pub. No. US2002/0058273 A1, May 16, 2002) and Goldschneider et al. (U.S. PG Pub. No. US 2002/0058791 A1, May 16, 2002) (hereinafter "Goldschneider").

With respect to claims 1 and 5, MacBeath teaches protein microarrays (protein chips) for high throughput function determination (see entire document). A variety of chemically derivatized slides (solid substrate) can be printed for example slides treated with aldehyde-containing silane reagent. The aldehydes can react readily with primary amines on the proteins. Protein microarray offer an ideal system, for example, for the rapid and parallel identification of substrates of protein kinases using protein microarray spotted with protein substrates such as kemptide (substrate peptide, p1762, 1<sup>st</sup> column, 2<sup>nd</sup> paragraph).

With respect to claim 6, MacBeath teaches a method for analyzing interaction between a reactive protein and the substrate peptide comprising the steps of:

- adding a reactive protein to the protein chip, the reactive protein showing a specific interaction with the substrate peptide immobilized on the protein chip (p1762, 2<sup>nd</sup> paragraph); and

- detecting the interaction between the reactive protein and the substrate peptide (p1762, 2<sup>nd</sup> paragraph).

However, MacBeath is silent on teaching that the substrate peptide is immobilized on the solid substrate by the mediation of a linker protein and the linker protein is fused with substrate peptides in the form of peptide monomer, a dimer of monomer-proline-monomer, or a multimer where monomers are linked to each other by a proline.

Inglese teaches reagents for linking proteins and substrate peptides (see entire document, particularly column 2, lines 11-26). The resulting compound is useful for many types of assays including high throughput screening assays (column 10, lines 6-11). Inglese further teaches the linker protein comprises leptin (column 13, lines 26-51). However, Inglese fails to teach that the linker protein is fused with substrate peptides in the form of peptide monomer, a dimer of monomer-proline-monomer, or a multimer where monomers are linked to each other by a proline.

Shipwash teaches that when it is necessary to reduce steric problems of an immobilized biomolecule, a suitable spacer arm may be used to immobilize the biomolecule to a surface (see entire document, particularly p22, paragraph [0264]). Suitable spacer arms may include, but are not limited to, carbon spacers, polyethylene glycol polymers, peptides, dextrans, proteins, and nucleic acids (p22, paragraph [0264]).

Goldschneider teaches proteins and polypeptides can be linked via variety of different type of molecules including peptides (peptide monomer) and bifunctional or

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chemical cross-linkers (see entire document, particularly pp2-3, paragraphs [0018] and [0019]).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ leptin of Inglese as the linker protein for substrate peptides in the protein microarray of MacBeath in order to immobilize small substrate peptides. The advantage of allowing small substrate peptides linked to protein molecules to be attached to the protein microarray surface without being obscured by BSA molecules, which are used to reduced nonspecific binding of other proteins by quenching unreacted aldehydes on the protein microarray surface as taught by MacBeath (p1760, 5<sup>th</sup> paragraph-p1760, 1<sup>st</sup> paragraph), provides the motivation to combine teachings of MacBeath and Inglese. In addition, one of ordinary skill in the art would have had a reasonable expectation of success in using protein-substrate peptides of Inglese for immobilization on the protein microarray since Shipwash teaches that when it is necessary to reduce steric problems of an immobilized biomolecule, a suitable spacer arm including proteins may be used to immobilize the biomolecule to a surface.

MacBeath in view of Inglese and Shipwash teaches the claimed invention except that the linker protein is fused with substrate peptides in the form of peptide monomer, a dimer of monomer-proline-monomer, or a multimer where monomers are linked to each other by a proline. Given that Goldschneider teaches both peptides (peptide monomer) or bifunctional or chemical cross-linkers can be used to link proteins and polypeptides, it would have been obvious to one of ordinary skill in the art to substitute



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one linking means for the other to achieve the predictable result of linking proteins and polypeptides.

10. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over MacBeath (*Science*, Sept. 8, 2000, Vol. 289, pp1760-1763) in view of Inglese (U.S. Patent No. 6,335,176 B1, Jan. 1, 2002), Shipwash (U.S. PG Pub. No. US2002/0058273 A1, May 16, 2002) and Goldschneider (U.S. PG Pub. No. US 2002/0058791 A1, May 16, 2002) as applied to claim 1 above, and further in view of Tsien et al. (U.S. PG Pub. No. US 2003/0186229 A1, published Oct. 2, 2003 and filed May 24, 2001) (hereinafter "Tsien").

MacBeath in view of Inglese, Shipwash, and Goldschneider teaches a protein chip of an S-L-SP form as set forth above. However, MacBeath in view of Inglese, Shipwash, and Goldschneider does not specifically teach that the peptide monomer is kemptide (SEQ ID NO:1).

Tsien teaches that kemptide can be used for linking proteins (see entire document, particularly p5, paragraphs [0046] and [0047]).

The rationale to support a conclusion that the claim would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. at \_\_\_, 82 USPQ2d at 1395; *Sakraida v. AG Pro, Inc.*, 425 U.S. 273, 282, 189 USPQ 449, 453 (1976); *Anderson's-Black Rock, Inc. v. Pavement Salvage Co.*, 396 U.S. 57, 62-63, 163

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USPQ 673, 675 (1969); *Great Atlantic & P. Tea Co. v. Supermarket Equipment Corp.*, 340 U.S. 147, 152, 87 USPQ 303, 306 (1950). “[I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does.” *KSR*, 550 U.S. at \_\_\_\_, 82 USPQ2d at 1396.

Given that the use of kemptide as a linker for proteins is known in the prior art (Tsien), one of ordinary skill in the art could have employed the kemptide of Tsien in order to link protein linker and peptide substrate of MacBeath in view of Inglese, Shipwash, and Goldschneider. The combination would have yielded nothing more than predictable results to one of ordinary skill in the art as Goldschneider teaches peptides (peptide monomer) can be used for linking proteins and polypeptides.

11. Claims 7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over MacBeath (Science, Sept. 8, 2000, Vol. 289, pp1760-1763) in view of Inglese (U.S. Patent No. 6,335,176 B1, Jan. 1, 2002), Shipwash (U.S. PG Pub. No. US2002/0058273 A1, May 16, 2002) and Goldschneider (U.S. PG Pub. No. US 2002/0058791 A1, May 16, 2002) as applied to claim 1 above, and further in view of Duffy (U.S. PG Pub. No. US 2002/0028463 A1, Mar. 7, 2002).

MacBeath in view of Inglese teaches a method of analyzing the interaction between a reactive protein and its substrate peptide using a protein chip of S-L-SP form as set forth above. However, MacBeath in view of Inglese fails to teach that the reactive protein is a fluorescent labeled antibody.

With respect to claims 7 and 9, Duffy teaches a protein chip of a S-L-SP form (see entire document, particularly Fig. 4), wherein a substrate peptide (SP, p5, paragraph [0046]) is immobilized on a solid substrate (S, array) by the mediation of a linker protein (L, streptavidin, p10, paragraph [0091] and Fig. 4). Duffy further teaches a method, wherein the reactive protein is an antibody labeled with fluorescent tags (pp4-5, paragraph [0038]).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to employ the fluorescent labeled antibody of Duffy as the reactive protein in the method of MacBeath in view of Inglese in order to detect the binding of the reactive protein to the substrate peptide. The advantage of directly detecting the binding of the reactive protein to the substrate peptide provides the motivation to combine teachings of MacBeath in view of Inglese and Duffy with a reasonable expectation of success.

### ***Allowable Subject Matter***

12. Claims 11 and 12 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: Claims 11 and 12 are directed to a protein chip of a S-L-SP form comprising a solid substrate (S) and a substrate peptide (SP) immobilized on the solid substrate (S) by a linker protein (L) of leptin or malic enzyme, wherein the SP is fused with L in the

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form of dimmer of monomer-proline-monomer and multimer-proline-multimer. Although the prior art teaches the SP is fused with L in the form of peptide monomer, the prior art fails to disclose that the SP is fused with L in the form of dimmer of monomer-proline-monomer and multimer-proline-multimer as recited in claims 11 and 12.

### ***Response to Arguments***

13. Applicant's arguments with respect to claims 1, 4-7, and 9 have been considered but are moot in view of the new ground(s) of rejection as set forth above.

Since the prior art fulfills all the limitations currently recited in the claims, the invention as currently recited would read upon the prior art.

### ***Conclusion***

14. Claims 1, 4-7, and 9 are rejected and claims 11 and 12 are objected.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to UNSU JUNG whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Unsu Jung/  
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Primary Examiner  
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